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to the binding of the compound in the absence of the plurality of compounds; and if so

- (4) separately determining the binding to the soluble polypeptide of each compound included in the plurality of compounds, so as to thereby determine whether a compound specifically binds to the soluble polypeptide of (a), (b) or (c).--

REMARKS

Claims 71 and 208-223 were pending in the subject application. By this Amendment, applicants have canceled claims 71, 210-212 and 215-217 without prejudice or disclaimer and amended claims 208, 209, 213, 214, 218, 221 and 222, and added new claims 224-228. Accordingly, upon entry of this Amendment, claims 208, 209, 213, 214 and 218-228, as amended, will be pending and under examination.

Applicants maintain that this Amendment raises no issue of new matter and is fully supported by the specification as filed.

Support for new claim 224 may be found inter alia in the specification, as originally-filed, on page 1, lines 16-32; page 20, lines 9-19; page 21, lines 3-7; and page 37, lines 27-32. Support for new claims 225 and 227 may be found inter alia in the specification, as originally-filed, on page 20, lines 23-25. Support for new claim 226 may be found inter alia in the specification, as originally-filed, on page 1, lines 16-32; page

20, lines 9-19; page 21, lines 3-7; and page 38, lines 19-31. Support for new claim 228 may be found inter alia in the specification, as originally-filed, on page 1, lines 16-32; page 20, lines 9-19; page 21, lines 3-7; and page 44, line 25 through page 45, line 17. Accordingly, applicants respectfully request that the Amendment be entered.

Title of the Invention

On page 2 of the July 28, 2000 Office Action the Examiner alleged that the title of the invention is not descriptive. The Examiner then required that a new title that is clearly indicative of the elected invention be submitted. The Examiner then suggested that the title be amended to recite "METHODS OF IDENTIFYING OR SCREENING FOR AGENTS THAT BIND THE OB-Re".

In response, in an attempt to advance the prosecution of the subject application, but without conceding the correctness of the Examiner's position applicants have amended the title to recite "METHODS OF IDENTIFYING OR SCREENING FOR AGENTS THAT BIND THE OB-Re".

Restriction Requirement

On page 2 of the July 28, 2000 Office Action the Examiner acknowledged Applicant's election with traverse of Group II. On page 4 of the July 28, 2000 Office Action, the Examiner alleged that newly submitted claims 221-223 are directed to an invention that is independent or distinct from the invention originally claimed. The Examiner further alleged that although there are no provisions under the section for "Relationship of Inventions" in

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MPEP 806.05 for multiple/different methods [original emphasis], restriction is deemed to be proper because the methods [original emphasis] appear to constitute patentably distinct inventions. The Examiner further alleged that the inventive concepts of the newly added method claims constitute Group IV, and that the methods of Group II and Group III require the use of different steps/methods; elements/agents that are physically and functionally distinct; that there are allegedly different starting elements and that the final outcome/results are different for these different methods that cover various diagnostic and therapeutic methods; and that if determined to be patentable they would also be patentably distinct. Furthermore, the Examiner alleged that these methods are not required one for the other, nor does each of these methods require the use of the product. The Examiner then concluded that because applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. The Examiner then stated that claims 221-223 are withdrawn from consideration as directed to a non-elected invention.

Applicants hereby admit on the record that the inventions identified by the Examiner as Groups II and IV are obvious over each other within the meaning of 35 U.S.C. §103 and maintain that restriction among the pending claims is not required.

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M.P.E.P. Section 803 states:

If there is an express admission that the claimed inventions are obvious over each other within the meaning of 35 U.S.C. §103, restriction should not be required. In re Lee, 199 USPQ 108 (Comm'r Pat. 1978).

Accordingly, applicants respectfully request that claims of Groups II and IV be examined together.

Rejection Under 35 U.S.C. § 112, second paragraph

On page 4 of the July 28, 2000 Office Action the Examiner rejected claims 71 and 208-220 under 35 U.S.C. §112, second paragraph, as indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

The Examiner alleged that claim 71 recites insufficient process steps, elements or limitation to achieve the claimed method because of the presence of the terms "contacting" and "under conditions suitable".

M.P.E.P. Section 2173.02 states:

The essential inquiry pertaining to this requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of:

- (A) The content of the particular application disclosure;
- (B) The teachings of the prior art; and
- (C) The claim interpretation that would

be given by one possessing the
ordinary level of skill in the
pertinent art at the time the
invention was made.

In an attempt to advance the prosecution of the subject application, but without conceding the correctness of the Examiner's position, applicants have canceled previous claim 71 and added new claim 224.

Applicants maintain that the language of claim 224 sets out and circumscribes a particular subject matter with a reasonable degree of clarity and particularity and thus fulfills the requirements of 35 U.S.C. §112, second paragraph. Applicants further maintain that the skilled artisan would readily understand the meaning of the word "contacting" and the phrase "under suitable conditions" based on the numerous examples, methods, and results taught in the specification of the pending application. Applicants specifically note page 61, line 5 through page 62, line 10; page 79, line 27 through page 80, line 3, and Figures 7a-7d of the specification, as originally filed, which describe an experiment in which the claimed polypeptide was "contacted" with a chemical compound (i.e., leptin) under "conditions suitable for binding" and the specific binding of the chemical compound was detected.

Applicants also maintain that the skilled artisan could readily ascertain the meaning of the word "contacting" and the phrase "under suitable conditions" in light of the teachings of the prior art.

On page 5 of the July 28, 2000 Office Action, the Examiner

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rejected claims 210 and 215 under 35 U.S.C. §112, second paragraph. The Examiner alleged that the terms "substantially the same" and "conditions suitable for binding" are viewed as relative and as such render the claims indefinite. Applicants initially note that the phrase "conditions suitable for binding" is not present in either of claims 210 or 215, thereby rendering this portion of the rejection moot. In addition, in an attempt to advance the prosecution of the subject application, but without conceding the correctness of the Examiner's position, applicants have canceled previous claims 210 and 215 and added new claims 225 and 227. New claims 225 and 227 do not recite either of the phrases in question, thereby rendering this portion of the rejection moot.

On page 5 of the July 28, 2001 Office Action the Examiner rejected claims 211 and 216 under 35 U.S.C. §112, second paragraph. The Examiner alleged that claims 211 and 216 are indefinite because they fail to point out what is included or excluded by the claim language. The Examiner further alleged that the claims are not further limiting in the statement that the "compound is not previously known to bind...".

In response, in an attempt to advance the prosecution of the subject application, but without conceding the correctness of the Examiner's position, applicants have canceled claims 211 and 216, thereby rendering this portion of the rejection moot.

On page 5 of the July 28, 2001 Office Action the Examiner rejected claims 212 and 216 and their dependent claims under 35 U.S.C.

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§112, second paragraph. The Examiner alleged that claims 212 and 216 and their dependent claims are prolix, whereby they contain long recitations or unimportant details which hide or obscure the invention. The Examiner also alleged that these claims comprise double inclusion of an element in members of Markush groups. Furthermore, the Examiner alleged that the claims represent an unreasonable number of claim limitations.

In response, in an attempt to advance the prosecution of the subject application, but without conceding the correctness of the Examiner's position, applicants have canceled claims 212, 216 and 217 and added new claims 224, 226 and 228.

Applicants maintain that new claims 224, 226 and 228 do not represent an unreasonable number of claim limitations. New claims 224, 226 and 228 define the soluble polypeptide by three sets of parameters. Applicants further maintain that the characterization of the soluble polypeptide in the claims is reasonable in light of the nature and scope of applicants' invention. In addition, new claim 228 recites a "first chemical compound" and a "second chemical compound" to clearly identify which chemical compound is at issue.

Applicants respectfully request that this rejection be withdrawn in light of the amendments and remarks made hereinabove.

Rejection under 35 U.S. 103(a)

On page 6 of the July 28, 2000 Office Action the Examiner rejected claims 71 and 208-220 under 35 U.S.C. 103(a) as unpatentable over

any one of Tartaglia, et al. ('621), Snodgrass, et al. ('123 or '098), Caskey, et al. ('340), Friedman, et al. ('335) or Chang, et al. ('424). The Examiner alleged that each of the references discloses the cloning and expression of one or multiple forms of the OB-R. The Examiner further alleged that each reference discloses that the receptors or cells that express these various forms of the OB-receptor can be used to detect for agents which bind to the receptor, wherein these detectable agents can be other variant forms of the receptor, or they can be for agonist or antagonist. The Examiner stated that Chang, et al. is the only reference which discloses an OB-R having an amino acid sequence that is identical to the claimed OB-R. The Examiner acknowledged that the references do not disclose the exact assay methods of the claims.

The Examiner then concluded that it would be prime facie obvious to detect for binding agents to the OB-R using any one of the receptors of the prior art, despite the fact that some of the prior art disclose the use of variant forms of the receptor. The Examiner further noted that even though applicants' claims refer to an OB-R of a specific sequence, there is nothing to suggest that the C-terminal portion of the OB-R is critical for the detection of the binding compounds and the only portion of the OB-R that is used to detect for the binding.

In response, applicants respectfully traverse the rejection under 35 U.S.C. §103(a) and maintain that the pending claims are patentable over Tartaglia, et al. ('621), Snodgrass, et al. ('123 or '098), Caskey, et al. ('340), Friedman, et al. ('335) or Chang,

et al. ('424) either alone or in combination with each other.

Applicants note that the OB-Re of the claimed invention is defined in the independent claims, as:

- (a) a soluble polypeptide comprising consecutive amino acids, the amino acid sequence of which is shown in Figure 5 (SEQ ID NO: 10);
- (b) a soluble polypeptide having a sequence which varies therefrom by no more than 15 amino acids, such variations:
 - (v) not involving amino acids corresponding to the amino acids at positions 799-804 of the amino acid sequence shown in Figure 5 (SEQ ID NO: 10); and
 - (vi) not changing the functional properties of the soluble polypeptide; or
- (c) a soluble polypeptide comprising the soluble polypeptide of (a) or (b) linked to consecutive amino acids corresponding to a flag epitope.

The OB-Re defined in the subject application is a "soluble" receptor, i.e., by sequence comparison to the Ob-R variants cited in the prior art, OB-Re lacks transmembrane domains and thus lacks an intracellular C-terminal tail. See page 1, lines 16-32 and Figures 6A-6B of the pending application. OB-Re is a "soluble" receptor because it is secreted from a cell into the extracellular domain. A method to detect binding agents to a soluble receptor would be different from that of a membrane-bound receptor. Thus,

a method to detect binding agents to the OB-Re would not be obvious from the teachings of Tartaglia et al ('621), Snodgrass et al ('123 or '098) or Caskey et al ('340) all of which disclose Ob-R variant polypeptide sequences which contain transmembrane domains and C-terminal tails, thereby defining those Ob-R variants as "cell-surface" receptors or "membrane-bound" receptors.

The soluble polypeptide of the claimed invention is not obvious over the three (3) mouse sequences disclosed by Friedman, et al. (labeled Friedman 1, Friedman, 2 and Friedman 3 on **Exhibit A** attached hereto) because these sequences do not disclose nor render obvious a soluble polypeptide as recited in the independent claims. As evidenced on Exhibit A, the three mouse sequences of Friedman, et al. differ significantly from the claimed soluble polypeptide. As noted on Exhibit A, those amino acids of the mouse sequences that are identical to the amino acid sequence of the claimed polypeptide are evidenced by a dot (.). Applicants maintain that the amino acid sequence of the claimed polypeptide differs significantly from the three (3) mouse sequences as Friedman, et al. and therefore the claimed polypeptide is not obvious over the three (3) mouse sequences of Friedman, et al.

The sequence of the OB-Re of Chang, et al. is identical to the amino acid sequence set forth in Figure 5 (SEQ ID NO: 10) of the subject application. Applicants note that PCT International Application No. WO 97/25424, published on July 17, 1997, i.e., less than one year before applicants' filing date. Attached hereto as **Exhibit B** is a copy of U.S. Serial NO. 08/582,825, filed January 4, 1996, the first priority document for WO 97/25424.

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Attached hereto as **Exhibit C** is a copy of U.S. Serial No. 08/774,414, the second priority document for WO 97/25424. Applicants have highlighted the subject matter that was presented for the first time in U.S. Serial No. 08/774,414, i.e., the subject matter that would not be entitled to the January 4, 1996 priority date. As evidenced therein, all disclosures of the soluble OB-Re and binding claims employing such a soluble OB-Re were added for the first time in the December 31, 1996 priority document. Accordingly, applicants maintain that WO 97/25424 (Chang, et al.) is effective as a reference against the claimed process only as of December 31, 1996.

As evidenced by the attached Declaration of Nika Adham, Beth Borowsky, Nigel Levens, and Radek C. Skoda under 37 C.F.R. §.131¹, (**Exhibit 1**) applicants had conceived and reduced to practice the claimed invention, specifically an embodiment claim 224 as amended hereinabove before December 31, 1996. Claim 224 recites a process for determining whether a chemical compound specifically binds to a soluble polypeptide. The Declaration specifically shows that prior to December 31, 1996, the Binding Assay was obtained by Noel Boyle under the direct supervision of coinventor Nika Adham in the United States at the laboratories of Synaptic Pharmaceutical Corporation, an assignee of record of the subject application.

Applicants maintain that in view of the Declaration, Chang, et al.

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The attached declaration has been signed only by Nika Adham. A declaration signed by all the inventors will be forwarded shortly.

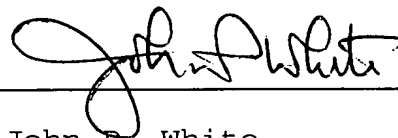
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should be withdrawn as a reference. Applicants further maintain that none of the remaining references disclose the Binding Assay as set forth in new claim 224. Accordingly, applicants respectfully request that this rejection be withdrawn.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided.

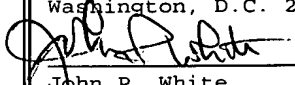
No additional fee, other than the fee for a three-month extension of time, is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.



John P. White
Reg. No. 28,678

1/29/01
Date